The University of Chicago

THE ATTEMPTED RESOLUTION OF A TERTIARY AMINE

A DISSERTATION SUBMITTED TO THE FACULTY
OF THE DIVISION OF THE PHYSICAL SCIENCES
IN CANDIDACY FOR THE DEGREE OF DOCTOR
OF PHILOSOPHY

DEPARTMENT OF CHEMISTRY
DECEMBER, 1945

By
ROBERT LEONARD ADELMAN

CHICAGO, ILLINOIS
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My deepest gratitude to Dr. M. S. Kharasch for his invaluable interest and advice during the course of the work.

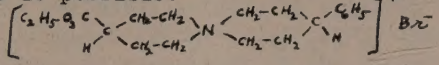
CONTENTS

		Page
I.	STATEMENT OF PROBLEM	1
II.	OBJECTIVES OF PRESENT STUDY	6
III.	EXPERIMENTAL APPROACH	8
IV.	EXPERIMENTAL DETAILS	10
	SUMMARY	24

I

STATEMENT OF PROBLEM

The distribution of the valencies in nitrogen compounds has been one of the most carefully investigated problems in stereochemistry. The arrangement of the atoms or groups about the nitrogen atom in quaternary ammonium compounds has been proved to be tetrahedral[1] rather than planar or pyramidal by showing that (1) the fifth valence of nitrogen is an electrovalence and the other four are covalences, (2) quaternary ammonium compounds with four different groups attached to the nitrogen are optically active, (3) the resolution of 4-phenyl,4'-carbethoxy bis piperidinium 1-1' spirane bromide is possible.



(If this compound were pyramidal, a plane of symmetry would exist, and no resolution would be possible.)

The configuration in amine oxides has also been proved to be tetrahedral[2] by resolution of compounds of the type $R_1R_2R_3NO$.

On the other hand, the spatial arrangement in trivalent nitrogen compounds has not been determined with certainty. There is a great deal of evidence to support the view that trivalent nitrogen has a pyramidal configuration (or tetrahedral if the assumption is made that the electron pair occupies the fourth corner of a tetrahedron).[3] Some of the evidence is as follows: (1) ammonia and amines possess definite dipole moments which are most readily explained by a non-planar distribution of the three valencies; (2) a nitrogen atom can replace a -CH group in aromatic compounds with no loss in stability, the replacing of a tetrahedral group by another group with no decided change in stability suggests a tetrahedral nitrogen atom; (3) X-ray data indicate that the nitrogen atom is at the peak of a three-sided pyramid

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[1] Henry Gilman, "Organic Chemistry," John Wiley and Sons, New York, 1st ed., 1938, I, 338-42.

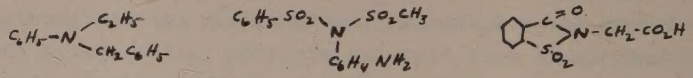
[2] Ibid., pp. 342-44.

[3] Ibid., pp. 336-38; 2d ed, 1942, I, 402-12.

with a carbon atom at each corner of the base in hexamethylenetetramine; (4) the existence of numerous pairs of syn and anti oximes, cis and trans azobenzene, and the like, can be explained only on the basis of a tetrahedral nitrogen atom; (5) electron diffraction data with trimethylamine and various other compounds of similar type; (6) spectroscopic evidence.

However, the direct chemical proof of the non-planar distribution of the three valencies of nitrogen in trisubstituted ammonia derivatives is lacking. Such proof would be the existence of optically active molecules of the type NR'R"R"'. Actually, all attempts to resolve such compounds, and also PR'R"R"' and AsR'R"R"',[4] have failed. These attempts extend over a period of fifty years, and their number reduces the probability that these molecules can be resolved under conditions as yet not investigated.

Workers in the field have been able to offer reasonable explanations for past failures, but have not been able to predict successful solutions of the problem. Thus the failure of early workers in their attempts to resolve secondary amines with d-tartaric acid can be explained by the formation of symmetrical cations of the ammonium type (NH R'R"). Many of the later failures were first explained by Meisenheimer[5] as being due to the ease with which the molecule undergoes optical inversion because of the rapid oscillation of the nitrogen atom through the plane of the substituents. Thus the larger the substituents and the lower the temperature, the easier should be the resolution.[6] However, types like the following could not be resolved.



Phillips pointed out that with tervalent sulfur compounds, the situation is similar, but separation of the enantiomorphs is possible. He states that the separation may be due to the fact that "the sulfur atom carries a positive formal charge, which may hold the electron shells of the atom more rigidly in position."[7]

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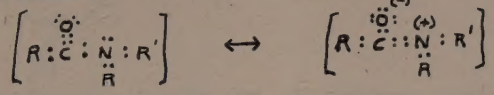
[4]Maitland, Ann. Repts. Chem. Soc., 36, 243 (1939).

[5]Meisenheimer, Angermann, Feinn, Vieweg, Ber., 57, 1747 (1924).

[6]Stewart and Allen, J.A.C.S., 54, 4027 (1932); Schreiber and Shriner, ibid., 57, 1896 (1935).

[7]Phillips, J.C.S., 127, 2552-60 (1925).

Pauling suggested that Meisenheimer's failures may be due to the wrong type of substituents on the nitrogen atom, that these substituents must not be phenyl or acyl, or any other electron acceptor type of group which would lead to a significant contribution of a resonance structure in which the groups attached to the nitrogen atom lie in a plane.[8]



It was then suggested that if it were possible to tie up the nitrogen atom in a rigid ring structure of some sort, it would be much more difficult for the nitrogen atom to invert its configuration. This view was supported by the data obtained from the infra-red absorption spectrum of ammonia. Kincaid and Henriques[9] calculated that the energy required to cause the nitrogen atom to pass through the plane of the hydrogen atoms is from 6 to 11 kilocalories per gram molecule. From much experimental evidence, it has been shown that for resolution at room temperature by ordinary methods, the energy of activation of the racemization must not be less than 20 to 25 kilocalories per gram molecule.[10] They thus conclude that NR'R''R''' is irresolvable unless the nitrogen forms part of a ring. A compound such as N-methyl ethyleneimine was calculated to have an activation energy of 38 kilo calories, and so compounds of this type should be resolvable.[11]

Meisenheimer,[12] Mole and Turner,[13] and Adams and Cairns[14] reached the same conclusion by another line of reasoning: when two of the three nitrogen valencies form a double bond, the third valency lies out of the plane of the other two, as shown by the existence of pairs of oximes, cis and trans azobenzene, and the stereochemical investigations of Mills. In asymmetric ethyleneimine derivatives the structure may be sufficiently rigid to sta-

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[8] Gilman, op. cit., 1st ed., I, 334.

[9] Kincaid and Henriques, J.A.C.S.; 62, 1474 (1940).

[10] Gilman, op. cit., 2d ed., I, 412.

[11] Kincaid and Henriques, op. cit.

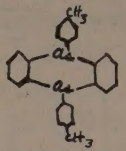
[12] Meisenheimer and Chou, Ann., 539, 70 (1939).

[13] Mole and Turner, Chem. and Ind., 582 (1939).

[14] Adams and Cairns, J.A.C.S., 61, 2464 (1939).

bilize the configuration of the nitrogen atom and allow resolution.

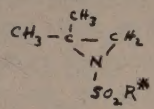
Kincaid and Henriques[15] also calculated that any trivalent asymmetric arsenic compound can be resolved, and their predictions have received verification in the work of Chatt and Mann,[16] in which two isomers of the compound



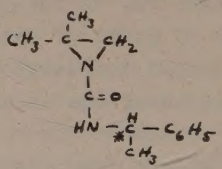
were isolated, proving the non-planar configuration of the trivalent arsenic atom.

Thus is seems highly desirable to attempt the resolution of rigid ring structures containing trivalent nitrogen, such as ethyleneimine derivatives.

Considerable difficulty was at first experienced in the preparation of substituted ethyleneimines.[17,18] However, in 1939, Adams and Cairns[19] made compounds of the type



in which an active sulfonyl group was substituted for the hydrogen atom on the nitrogen. Their attempts to make the compounds R^* - d-camphor or d-bromo camphor resulted in oils. Cairns[20] in 1941 prepared 2,2-dimethyl ethyleneimine in satisfactory quantities from compounds of the type $R_2C(NH_2)CH_2OH$ rather than from substituted ethanol amines of the type $R_2CHOHCH_2NH_2$. The latter tend to lead to substituted allylamines or vinyl amines. The 2,2-dimethyl—ethyleneimine was treated with 1-∝phenyl ethyl isocyanate to form a urea derivative.



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[15] Kincaid and Henriques, op. cit.

[16] Chatt and Mann, J.C.S., 142, 1184 (1940).

[17] Meisenheimer and Chou, op. cit.

[18] Mole and Turner, op. cit. [19] Adams and Cairns, op. cit.

[20] Cairns, J.A.C.S., 63, 871 (1941).

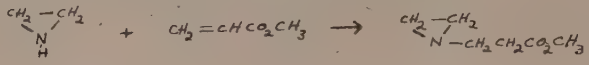
This derivative was subjected to fractional crystallization, but no evidence of separation into diasterioisomers was obtained. However, Cairns recognized Pauling's observation that there are objections to a compound having a carbonyl or sulfonyl group directly attached to the nitrogen atom, as previously mentioned.

II

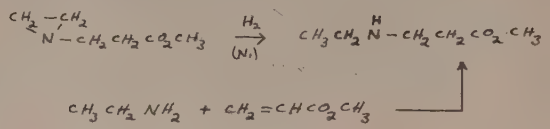
OBJECTIVES OF PRESENT STUDY

This work was undertaken to investigate the preparation and properties of ethyleneimine derivatives having the following characteristics: (1) the molecule would be asymmetric if the nitrogen atom was rigidly held, (2) an active group capable of reacting with optically active reagents isolated from the "asymmetric" nitrogen atom to reduce the resonance effect described by Pauling, as mentioned on page 3 above.

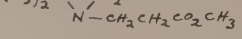
It was found that ethyleneimine, under very mild conditions, will add to methyl acrylate to form β-ethylene imino propionic acid methyl ester in quantitative yields.



This compound has not been described previously. The structure assigned to this imino acid ester has been confirmed by hydrogenation. The resulting product was proved to be identical with β-ethylamino propionic acid methyl ester prepared from ethylamine and methyl acrylate.



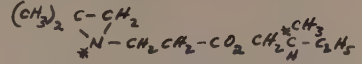
It was then seen that a compound of the type of β-(2,2-dimethylethylene imino) propionic acid methyl ester



is an asymmetric molecule (providing the configuration of the nitrogen atom is fixed), and also has an active group satisfactorily distant from the "asymmetric" nitrogen atom, and so the attempt was made to resolve the compound.

As the molecule is quite small and so is fairly volatile,

it was decided to form the active amyl ester of the β imino acid, and attempt to separate the resulting diastereoisomers by fractional distillation.



Bailey and Hass[21] have separated the diastereoisomers of dl-2-methyl butanoic acid d-2-methyl l-butanol ester, d-lactic acid dl-2-pentanol ester, and others, by fractional distillation. Phillips[22] also used fractional distillation in the separation of the diastereoisomers of l-β octyl p-toluene sulphinate. It was hoped that at least a measurable degree of separation might be attained by this method, provided of course that no racemization, decomposition, or the like occurred during the distillation. Active amyl alcohol was chosen as the optically active reagent because of its low boiling point and its ease of preparation.

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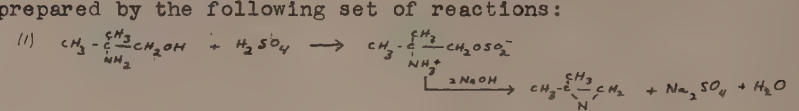
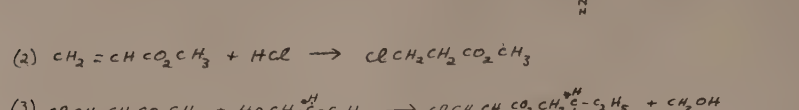
[21] Bailey and Hass, J.A.C.S., 63, 1969 (1941).
[22] Phillips, J.C.S., 127, 2560 (1925).

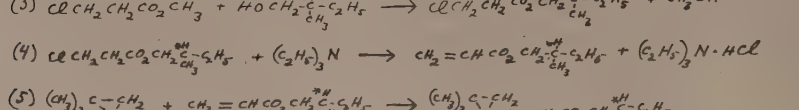
III

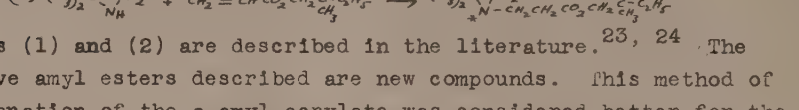
EXPERIMENTAL APPROACH

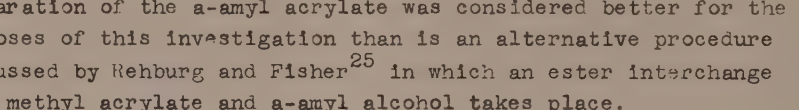
β-(2,2-dimethylethyleneimino) propionic acid a-amyl ester was prepared by the following set of reactions:











Steps (1) and (2) are described in the literature.[23, 24] The active amyl esters described are new compounds. This method of preparation of the a-amyl acrylate was considered better for the purposes of this investigation than is an alternative procedure discussed by Rehburg and Fisher[25] in which an ester interchange with methyl acrylate and a-amyl alcohol takes place.

Their method was found not suitable for the preparation of a-amyl acrylate for the following reasons: (1) the data of Rehburg and Fisher indicate that in the preparation of isoamyl acrylate the yields are not quantitative based on the alcohol used (87%); (2) as the reaction is not quantitative, the a-amyl acrylate product would then be contaminated with some unchanged a-amyl alcohol. As the alcohol and the corresponding acrylate boil only 20°-25°

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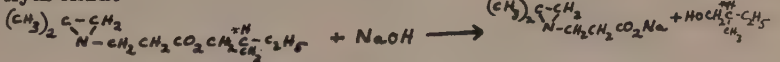
[23] Cairns, op. cit.

[24] V. Richter, "Organic Chemistry," E. Smith translation, Blakiston's Sons and Co., Philadelphia, 1913, I, 280. (The addition of hydrochloric acid to only acrylic acid is described in the literature.)

[25] Rehburg and Fisher, J.A.C.S., 66, 1203 (1944).

apart at atmospheric pressure the problem of obtaining the pure a-amyl acrylate without any optically active impurities would become important; (3) in a trial run using the Rehburg and Fisher method with isoamyl alcohol, over 10% polymerization of the isoamyl acrylate product was observed.

The a-amyl β (2,2-dimethylethyleneimino) propionate was prepared by mixing equimolar quantities of the imine and the acrylate, and heating at 40°-50°C. for extended periods. The crude product was then carefully fractionated under reduced pressure, samples were taken and their rotation measured. These samples were then refractionated to note if any change in rotation or any drift could be observed. After the second refractionation the samples had, within experimental limits, the same rotation. Furthermore the sodium salt of β (2,2-dimethylethyleneimino) propionic acid prepared by saponification of the a-amyl ester with sodium hydroxide



was observed to have no rotation. Thus no separation had been effected.

There are of course many possible explanations for the failure to obtain a separation. However, until further work is done on this problem it is futile to speculate upon the possible sources of error.

IV

EXPERIMENTAL DETAILS

(1) β - Ethyleneimino Propionic Acid Methyl Ester

One mole of methyl acrylate (B.P. 79°-80°, 86 grams) was added drop by drop to one mole of ethyleneimine (B.P. 56°-58°, 43 grams) which was well stirred and cooled to 0°-5°C. The resulting solution was allowed to stand for ten hours at room temperature and then was distilled at reduced pressure. One hundred twenty grams (92% yield) of pure product boiling at 61°-64° at 10 mms. pressure was obtained. The percentage of nitrogen found (Dr. T. S. Ma) was 10.79. The percentage of nitrogen calculated is 10.85. The refractive index was $n_D^{21°} = 1.4363$. Conclusive proof of structure was shown as follows: (a) No reaction occurred with phenyl isothiocyanate, which indicates the presence of a tertiary amino nitrogen. (b) On hydrogenation of 1/3 of a mole (43 grams) in 150 mls. of dioxane, with 4 grams of Raney nickel as catalyst, 150 atmospheres of hydrogen pressure, and at 100°C. for 2 hours, 1/3 of a mole of hydrogen was taken up. Twenty-eight grams (64% yield) of hydrogenated product boiling at 78°-79° at 29 mms. pressure was obtained, with the refractive index as $n_D^{20} = 1.4260$. A thiourea with phenyl isothiocyanate was easily formed, which melted sharply at 120.5°-121°. No previous mention of the hydrogenation of any ethyleneimino derivatives could be found in the literature. This hydrogenated product was proved to be identical with β-ethylamino propionic acid methyl ester, which was independently prepared by the addition of 0.4 mole (34 grams.) of methyl acrylate drop by drop to a well-stirred solution of 0.42 moles (18.6 grams) of ethyl amine in 400 mls. of pure methanol kept at 0°-5° during the addition. After stirring for two hours at room temperature, the methanol was taken off at atmospheric pressure, and the product was distilled under reduced pressure. Thirty-five grams (67%) of pure product was obtained (B.P. 82°-83° at 31 mms. pressure and $n_D^{20} = 1.4250$). On reaction with phenyl isothiocyanate, the resulting thiourea melted at 120.5°-121°. Mixed melting

points with the hydrogenation product resulted in no melting point depression.

(This method of preparation of β-ethylamino propionic acid methyl ester is somewhat similar to the method described by Morsch[26] for the preparation of β-methyl-amino propionic acid methyl ester, although a maximum of only 39% yields was obtained by his methods.)

(2) 2,2-Dimethyl Ethyleneimine

Two hundred grams (2 moles) of sulfuric acid in 400 mls. of water were added slowly to 180 grams (2 moles) of 2-methyl 2-amino 1 propanol (Commercial Solvents product) dissolved in 300 mls. of water, with rapid swirling of the flask. The flask was then attached to a condenser set for distillation, and heated up to 115°-120°. The pressure was reduced to 10 mms., and the reaction flask was heated up to 150°-165° for one hour. After cooling down to room temperature the flask was broken, and the product was well pulverized. The product was then added to 200 grams (5 moles) of sodium hydroxide dissolved in 300 grams of water, and the mixture was distilled at atmospheric pressure until the temperature of the vapors rose to 98°. The distillate was treated with sodium hydroxide pellets, and the upper amine layer was separated. The crude product was dried three times with fresh potassium hydroxide, and then with sodium. The product was then distilled through a Vigreoux column and then through a Podbielniak column. Ninety grams of pure product boiling at 71.5°-71.8° (63% yield) were obtained, $n_D^{22} = 1.4067$. Cairns[27] obtained only 50% yields using the same general procedure. Careful drying and pulverizing of the amine salt is essential for good yields.

(3) β-(2,2-Dimethyl Ethyleneimino) Propionic Acid Methyl Ester

Forty-three grams (1/2 mole) of methyl acrylate were mixed with 35.5 grams (1/2 mole) of 2,2-dimethylethyleneimine and warmed to 45° for ten minutes. The solution was then allowed to stand overnight at room temperature. Forty-seven grams of product (60% yield) boiling at 75°-77° at 8 mms. pressure, $n_D^{19.5} = 1.4398$ were obtained.

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[26] Morsch, Monatsch, 63, 220 (1933).

[27] Cairns, op. cit.

(4) Methyl β-Chloropropionate

Seventy-five grams (2.1 moles) of anhydrous hydrogen chloride were slowly passed into 172 grams (2 moles) of methyl acrylate (Commercial, stabilized with hydroquinone), and the temperature during the addition was kept at 25°-35°C. The resulting solution was allowed to stand for 24 hours at room temperature, and was then distilled at reduced pressure. After 2-3 grams of fore-run, 225 grams of product (93% yield) distilled at 42°-45° at 15 mms. pressure. $n_D^{21°} = 1.4262$.

(5) Active Amyl Alcohol

Fusel oil was carefully fractionated to obtain the active amyl alcohol. The refined fusel oil was obtained from the United States Industrial Chemical Company, and was dried with calcium chloride for 48 hours. Three-liter batches were fractionated at a time in the 100 plate column described on page 9. Small fractions were collected and tested by refractive index and optical rotation. The reflux ratio was about 15-20 to 1. The rate of takeoff was about 8-10 ml. per hour. The data from one run are indicated in Table 1 on the following page.

A total of about 7 liters of fusel oil was fractionated as described in Table 1. All of the samples with $n_D^{21°} = 1.4050$ or greater were combined, and redistilled in a 6-foot Podbielniak Hyper-Cal column (rated at 100-200 plates). The take-off was adjusted to about 5-8 mls. per hour, with a reflux ratio of 50 to 1, to 100 to 1. The final fractionation data are described below in Table 2 (see page 14).

TABLE 1

FIRST FRACTIONATION OF FUSEL OIL

Sample	Quantity	Boiling Point	Refractive Index	Rotation
1.....	100 ml.	108°C.	$n_D^{21.5°} = 1.3938$	...
2.....	100	108°-113°	$n_D^{21.5°} = 1.3962$	...
3.....	50	113°-126°	$n_D^{21.5°} = 1.4011$	...
4.....	75	128°-130°	$n_D^{21.5°} = 1.4069$	...
5.....	50	130°	$n_D^{22°} = 1.4082$	...
6.....	50	130°	$n_D^{21°} = 1.4085$	...
7.....	70	130°	$n_D^{21°} = 1.4090$	-4.5°/1 dm.
8.....	40	130°	$n_D^{21.5°} = 1.4090$	...
9.....	40	130.2°	$n_D^{23°} = 1.4083$	...
10.....	80	130.2º130.6°	$n_D^{23°} = 1.4082$	...
11.....	50	130.3º130.4°	$n_D^{23°} = 1.4082$	...
12.....	80	130.5º130.7°	$n_D^{23.5°} = 1.4077$	...
13.....	50	130.7º131.0°	$n_D^{23.5°} = 1.4077$	...
14.....	50	131°	$n_D^{24°} = 1.4071$	...
15.....	50	131°	$n_D^{24°} = 1.4073$	-3.0°/1 dm.

TABLE 2

FINAL FRACTIONATION OF FUSEL OIL

	Quantity	Boiling Point	Refractive Index	Rotation
1...	40 ml.	124°-128°	$n_D^{23} = 1.4013$	...
2...	50	128°-131°	$n_D^{23} = 1.4086$	...
3...	110	131°	$n_D^{23} = 1.4089$	4.6°/Dm.(27°C)
4...	60	131°	$n_D^{23} = 1.4090$	...
5...	50	131°	$n_D^{24} = 1.4091$	4.65°/Dm.
6...	100	131°	$n_D^{24} = 1.4088$	...
7...	60	131°	$n_D^{24} = 1.4089$	4.70°/Dm.(27°C)
8...	40	131°	$n_D^{24} = 1.4087$	...
9...	70	131°	$n_D^{24} = 1.4087$	...

It was found that the rotation increases about .05° per decimeter for every 1°C. lowering in temperature of the sample in the polarimeter tube.

Fractions (3) through (9) were combined, and dried with Drierite. The refractive index was $n_D^{20°} = 1.4108$, the density was 0.816, and optical rotation was -18.60°/4 dms. at 25°C. Thus $[\alpha]_D^{25} = -5.70$, or the calculated value for 20°C. is $[\alpha]_D^{20} = -5.93°$. Whitmore and Olewine's data are $n_D^{20°} = 1.4110$, the density was 0.816, and $[\alpha]_D^{20} = -5.90°$.[28] Three hundred fifty to four hundred grams of pure active amyl alcohol were obtained from 7 liters of fusel oil.

(5) β-Chloro Propionic Acid Active Amyl Ester

One hundred seventy grams (1.94 moles) of active amyl alcohol were mixed with 246 grams (2 moles) of methyl β-chloro propionate in 1 liter of dry benzene. Two mls. of concentrated

[28] Whitmore and Olewine, J.A.C.S., 60, 2569 (1938).

sulfuric acid were added, and the solution was heated to reflux in a column packed with glass helices and fitted with a variable take-off head. The benzene-methyl alcohol azeotrope was removed at 58°-60°. (The bath temperature reached 130° at the end of the reaction.) One hundred eighty-five grams of azeotrope were removed. The remaining solution was then rapidly distilled under reduced pressure. Two hundred ninety grams of product (87% yield) boiling at 89°-91°/10-12 mms. were obtained. This was refractionated carefully in a Podbielniak column to make sure that all the fractions had the same rotation. The fractionation data are described in Table 3 on the following page.

(6) Active Amyl Acrylate

Preliminary experiments on the dehydrohalogenation of a-amyl β chloro propionate with triethylamine with benzene as the solvent, resulted in only a 60% conversion after heating the solution to reflux for $1\frac{1}{2}$ hours. When toluene was used as the solvent in order to get a higher reaction temperature, almost a quantitative yield of the dehydrohalogenated product was obtained. Thus a large-scale preparation of a-amyl acrylate was carried out as follows: 170 grams (1 mole) of a-amyl β chloro propionate were dissolved in a solution of 8 grams of hydroquinone in 200 grams of dry toluene. Two hundred grams (2 moles) of triethyl amine (dried over sodium hydroxide, Drierite, and distilled) were added at once. The solution was heated to reflux (100°-120°C.) for 1 hour. A heavy precipitate of triethyl amine hydrochloride was formed. The mixture was allowed to cool to room temperature. The precipitate was washed with 200 grams of toluene, and the washings were added to the filtrate. Another 8 grams of hydroquinone were added, and the solution was distilled at reduced pressure through a Vigreaux column. One hundred fifteen grams of crude product (80% yield) boiling at 70-80°/45 mms. were obtained. No residue in the distilling flask beside the hydroquinone was observed. The crude a-amyl acrylate (160 grams) was then carefully distilled through a Podbielniak column. Four portions of about 40 mls. each were collected. The data are described in Table 4 on page 16. From Table 4 it can be seen that fraction (4) is the most nearly pure, and that 1%-4% of unchanged β chloro acid ester was carried over in the more rapid distillations. However, this impurity boils sufficiently far from the final prod-

TABLE 3

FRACTIONATION OF ACTIVE AMYL β CHLORO PROPIONATE

	Boiling Point	Refractive Index	Rotation	Density	Specific Rotation
1...	89.8-90°/10 mms.	$n_D^{21} = 1.4347$	+13.04°/4 Dms. at 21.7° C.	1.0224/22°C.	$(\alpha)_D^{22} = +3.190° \pm .008°$
2...	89.8°-90°/10 mms.	$n_D^{21} = 1.4348$	+13.02°/4 Dms. at 21.7° C.	...	...
3...	89.8°-90°/10 mms.	$n_D^{21} = 1.4349$	+13.07°/4 Dms. at 21.7° C.	...	...
4...	89.8°-90°/10 mms.	$n_D^{21} = 1.4349$	+13.03°/4 Dms. at 21.7° C.	...	...
5...	89.8°-90°/10 mms.	$n_D^{21} = 1.4349$	...	...	...

TABLE 4

FRACTIONATION OF ACTIVE AMYL ACRYLATE

	Boiling Point	Distillation Rate	Refractive Index	Rotation	Density
1....	63°/21 mms.	10 cc/hr.	$n_D^{20.5}$ = 1.4242	+20.56°/4 dm.(22.3°C.)	...
2....	63°/21 mms.	20 cc/hr.	$n_D^{20.4}$ = 1.4259	+20.17°/4 dm. (22.3°C.)	...
3....	63°/21 mms.	20 cc/hr.	$n_D^{20.2}$ = 1.4253	+20.47°/4 dm. (22.3°C.)	...
4....	63°/21 mms.	10 cc/hr.	$n_D^{20.2}$ = 1.4237	+20.91°/4 dm.(22.3°C.)	.887(20.6°C.)

uct so that it was separated easily in the next step by careful fractionation. In order to prevent polymerization of the acrylate, 5 grams of hydroquinone were added to the still pot, and the system was flushed out with nitrogen before beginning the distillation. No polymerization was observed.

(7) Active Amyl β (2,2 Dimethylethyleneimino Propionate

Seventy-four grams (1.04 moles) of 2,2 dimethylethyleneimine were mixed with 140 grams (.985 moles) of a-amyl acrylate containing 2 grams of hydroquinone. A homogeneous solution resulted, and no heat effect was observed. The solution was heated 1 hour at 45°, and then allowed to stand 2 days at room temperature. The resulting solution was then distilled with an oil pump at .3 mm. pressure. Unchanged imine and acrylate were first collected in a trap. The product then distilled at 82°-87°/.3mm. Only a 20% yield (42 grams) was obtained, but recovery of the unchanged imine and acrylate was quantitative.

The unreacted materials were recombined, another 2 grams of hydroquinone were added, and the solution was heated to 40°-45° for 16 hours over a 72-hour period. A 35% yield of product was obtained, with a quantitative recovery of unchanged material. With a sample standing at 30°-35° for three weeks, a 60% yield of product was obtained, with quantitative recovery of unchanged starting materials.

The additions were discontinued after about 175 grams (83% yield) of product were obtained. Twenty-two grams of unchanged imine and acrylate remained. Over 94% of the starting material was accounted for.

The physical constants on the crude product were as follows: Boiling point 82°-87°/0.3 mm, $n_D^{19} = 1.4399$, rotation $= +9.18°$ at 22°C. for a 4 DM tube, density $= 0.914$ at 22°C.

One hundred seventy-five grams of the crude product were then carefully fractionated under reduced pressure in a 100 cm. Podbielniak "Heli-Grid" column with a heated, non-silvered vacuum jacket. This column rated well over 100 theoretical plates at atmospheric pressure, as was evidenced in the separation of a-amyl alcohol from fusel oil. A more efficient separation of the a-amyl alcohol was obtained with this column than was obtained with the rated 100 plate Fenske-type column used by Whitmore and

Olewine[29] for the same purpose.

It is desirable to have the fractionation temperature as low as possible to prevent diasterioisomer interconversion. On the other hand, the performance of the column begins to suffer at pressures below 20 mms.[30] As a compromise, a boiling point of 115° -120° at a pressure of 8-10 mms. was decided upon as the working range. The manostat held the pressure to within variations of 1 mm. It was found necessary to superheat the column somewhat to compensate for the large pressure drop in the column due to the low operating pressure. Without the high column jacket temperature (145°-150°) a tendency toward excessive holdup was observed and strong heating of the liquid in the still pot (over 160°C.) would have been necessary to drive the vapors through the column.

Thirty to forty ml. samples were collected, and the rotation of each was measured in a 4-dm. tube. There was no change of rotation with time. All the samples were allowed to stand in the polarimeter tube until temperature equilibrium was reached (1/2-1 hour). The polarimeter tube used for all the measurements was of the type filled from the side to cancel any errors due to optical anisotropy of the end glasses.[31] There were no observable changes in boiling point, refractive index, or density in the refractionated samples. No decomposition during fractionation was observed.

A total of 175 grams of the crude product was used for the final careful fractionations. The first fractionation was not too significant, as the product had to be separated from small amounts of a-amyl acrylate and a-amyl β-chloro propionate. The data on fractionation (A) are described on Table 5 on the following page.

Each fraction was 30-40 mls., except (f), which was 10 mls. The pot temperature was 135°-140°, column temperature was 140°, reflux ratio was 20:1, and the take-off was 5 ml. per hour.

In the next fractionation (fractionation B) samples (a), (b), and (c) were combined to make 90-100 mls. of liquid, and two first 40 ml. portions (samples [g] and [h]) were collected. The data on fractionation (B) are described on Table 6 (page 21 below).

The temperature conditions for the fractionation were the same as for fractionation (A). The reflux ratio was increased

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[29] Ibid.

[30] Podbielniak, Ind. Eng. Chem. A. E., 5, 121 (1933); 13, 639 (1941); Selker, ibid., 12, 352 (1940).

[31] Davis and Ackerman, J.A.C.S., 67, 488 (1945).

TABLE 5

FRACTIONATION (A) OF ACTIVE AMYL β (2,2 DIMETHYLETHYLENEIMINO) PROPIONATE

	Boiling Point	Refractive Index	Rotation	Density
a.....	118.5°/8 mms.	$n_D^{19.5}$ = 1.4398	+9.09°/4dm. at 21.8°C.	0.910 at 20°C.
b.....	118.5°/8 mms.	$n_D^{19.5}$ = 1.4398	+8.92°/4dm. at 21.8°C.	...
c.....	120°/8 mms.	$n_D^{19.5}$ = 1.4398	...	...
d.....	120°/8 mms.	$n_D^{19.5}$ = 1.4398	...	0.910 at 20°C.
e.....	120°/8 mms.	$n_D^{19.5}$ = 1.4397	+8.88°/4dm. at 20.8°C.	...
f.....	120°/8 mms.	$n_D^{19.5}$ = 1.4398	...	0.910 at 20°C.

TABLE 6

FRACTIONATION (B) OF ACTIVE AMYL β (2,2-DIMETHYLETHYLENEIMINO) PROPIONATE

	Boiling Point	Refractive Index	Rotation	Density
g.....	119°/8 mms.	$n_D^{19} = 1.4400$ $n_D^{19.5} = 1.4398$	+8.99°/4 dms./21.2° C.	0.910 at 20° C.
h.....	119°/8 mms.	$n_D^{19.5} = 1.4398$	+8.96°/4 dms./21.2 C.	...

to 30:1, and the rate of take-off decreased to 2-1/2 mls. per hour.

In fractionation (C), samples (d), (e), and (f) from fractionation (A) were combined, and refractionated under the same conditions as for fractionation (B). The results are shown in Table 7.

TABLE 7

FRACTIONATION (C) OF ACTIVE AMYL β (2,2-DIMETHYLETHYLENEIMINO) PROPIONATE

	Boiling Point	Refractive Index	Rotation
i....	119°/8 mms.	$n_D^{19.5} = 1.4398$	+8.94/4 dm / 21.3° C.
j....	119°/8 mms.	...	+8.95/4 dm / 21.4° C.

In fractionation (D), sample (g) from fractionation (B) was refractionated, and the first 25 mls. were taken (k). The rotation of this sample was found to be +8.92° per 4 dms. per 23° C.

In fractionation (E), sample (j) from fractionation (C) was refractionated, and the last 25 mls. were taken (ℓ). The rotations of this sample were found to be +8.95° per 4 dms. per 21.7° C. and +8.97° per 4 dms. per 21.0 C. Enough readings were taken so that the variation of the rotation with temperature is probably a real one. This variation amounts to an increase of .02° per 4 dms. in rotation for a .7°C. decrease of temperature. Then a correction of the rotation of sample (k) to 21.6°C. would result in a rotation of 8.96° ± .02° per 4 dms. per 21.6° C. Thus the rotations of (k) and (ℓ) are identical within experimental error.

In making the polarimeter readings, no reading differed from any other (for any particular sample in question) by more than .06° per 4 dms. Enough readings were obtained to get a precision of .01° per 4 dms. The rotations are accurate to .02° per 4 dms., as they are each subtracted from the experimental zero point of the polarimeter.

The polarimeter was made by Schmidt and Haensch.

The percentage of nitrogen found for sample k was 6.72 (Dr. T. S. Ma). The calculated percentage of nitrogen is 6.57.

It was also found that no hydrogenation occurred with these ethyleneimino derivatives under a pressure of 3 atmospheres of hydrogen, using Raney nickel as catalyst.

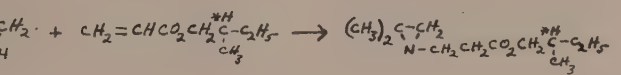
(8) Sodium β(2,2-Dimethyl ethyleneimino) Propionate

Four and two-tenths grams (0.02 mole) of β(2,2-dimethyl ethyleneimino) propionic acid a-amyl ester (sample k) in 25 ml. absolute ethanol were mixed with .8 gram (.02 mole) of sodium hydroxide prepared in 25 ml. absolute ethanol. After the mixture had stood 16 hours at room temperature the excess ethanol and a-amyl alcohol were removed by evaporation at reduced pressure (20 mms.) at 50°C. The residue was taken up in ethanol and re-evacuated to dryness. This residue was then dissolved in 30 ml. of absolute ethanol, and its rotation measured. Zero rotation was observed.

An examination of the data also shows, that in a comparison of the rates of addition of ethyleneimines to the unsaturated esters under similar experimental conditions,

(a)

(b)

(c) 

(a) is greater than (b) which is greater than (c).

SUMMARY

1. Several different esters related to β ethyleneimino propionic acid and β (2,2-dimethylethyleneimino) propionic acid were prepared and some of their properties noted.

2. The structure of this type of compound was proved.

3. The attempted resolution of β (2,2-dimethylethyleneimino) propionic acid a-amyl ester failed.

4. Improvements in the preparation of several types of compounds were made.